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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,818	02/27/2004	Prabha Ibrahim	039363-1202	5635

30542 7590 02/06/2007

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EXAMINER	
NASHED, NASHAAT T	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,818	IBRAHIM ET AL.	
	Examiner	Art Unit	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-66 and 72-104* is/are pending in the application.

4a) Of the above claim(s) *17-54,56-65 and 88-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-16,55,66,72-87 and 99-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/18/06; 12/18/06 & 11/22/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The application has been amended as requested in the communication filed October 25, 2006. Accordingly, claims 1, 2, 7, 8, 12, 14, 16, 55, 66, 72, 74, 75, 78-81, 83, and 92 have been amended; claims 3, 4, 67-71, and 96 have been canceled and new claims 99-104 have been added.

Amended claims 92-95, 97, and 98 are directed to non-elected invention of Group III. See the previous Office action, mailed June 22, 2006. Also, claim 66 contains a restrictable subject matter. The elected invention is directed to a method of identifying compounds that binds PYK2. This does not include methods of identifying mutation sites or attachments sites for derivatization. The methods of identifying compounds that binds to PYK2, mutation sites, and attachment sites are independent methods having different steps and products, and therefore, would require separate searches in the patent and non-patent literature. Thus, claims 92-95, 97, and 98 have been withdrawn from further consideration, and claim 66 is examined to the extent of identifying antigenic epitope.

Claims 1, 2, 5-16, 55, 66 (in part), 72-87, and 99-107 are under consideration.

Claim 66 is objected to because it contain non-elected subject matter.

The disclosure is objected to because of the following informalities: In Table 5 (now Table 3), the parameters in the two equations are not defined as well as parameters in the top raw of the Table. For example, while V_{max} has a well-established meaning in the art, i.e., k_{cat} [E] where [E] is the enzyme concentration, V_{max} (SE) is not. Also, K, K(SE), K(lo 95%), and K(up 95%) are undefined without an established definition for them in the prior art.

In response to the above objection, applicants argue that, similar to V_{max}, all other parameters are well known in the prior art and cite a commercially available curve-fitting program.

Applicants' arguments filed 12/4/2006 have been fully considered, but they are found unpersuasive. Applicants are correct that the terms K_i, K_d, and IC_{50} are well known in the prior art and their definition can be found in any introductory biochemistry textbook. The other abbreviations, however, are not well-accepted notation as they could be notations used by the specific computer package the applicants have. The examiner is not aware of a statistical factor named "standard error" or its abbreviation "SE", but "standard deviation" or "sd" is a well-appreciated term in the art.

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the newly filed drawing of Figures 3 and 4D remain of law quality and hard to read. In particular, the lettering of Figure 3 is too small and the solid black boxes in the figure should be replaced with a transparent box so that the writing inside the box could be seen. Figure 4D intended to show 60 bases/line. For example,

residues 1381-1440 should be all on the same line. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

> The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 5-16, 55, 66, 72, 78-87, and 99-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons set forth in the prior Office action mailed June 22, 2006.

In response to the above rejection, applicants disagree with the examiner's assessment of the written description and argue that claim 1 summarizes the invention and other independent claims provide similar steps. Also, applicant referred to paragraphs 64 and 65 of the specification as a support for both general and specific crystals.

Applicants arguments filed 10/25/06 have been fully considered, but they are found unpersuasive. As indicated in the previous Office action, the claims are directed to any method utilizing any structure obtained by any method including any crystallographic method using any crystal containing any protein named PYK2. Paragraph 64 describe the crystallization of a generic protein named PYK2, whereas paragraph 65 describe a generic crystallization screening method to obtain a crystal to some generic PYK2 protein. In fact, paragraph 65 supports the examiner rejection by providing evidence that the applicants did not have position of any other crystals of PYK2 at the time of invention. Describing a general method used in the art to obtain an invention is not sufficient showing of position of the invention. Besides disagreeing with the examiner rejection, applicants have not provided any evidence showing that the specification fully describes the genus encompassing the claimed invention. The description of a single species is not sufficient description of an entire genus. New claims 99-104 are included in this rejection because they are drawn to a genus of embodiment. Claims 99 and 100 limit claim 1 to using a crystallization kit to identify a crystal in order to obtain the structure information. Claims 101 and 102 limit claim 1 to obtaining co-crystal from a range of crystallization conditions. The specification does not teach that a co-crystal was obtained under any condition within the range. Claims 103 and 104 limit the claim to any fragment of at least 50 amino acid residues having 90% sequence homology to SEQ ID NO: 1, but the specification does not teach any

crystal of at least 50 amino acid residues of SEQ ID NO: 1 other than that of SEQ ID NO: 1.

Claims 1, 2, 5-16, 55, 66, 72, 78-87, and 99-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for the reasons set forth in the prior Office action mailed June 22, 2006.

In response to the above rejection, applicants disagree with the examiner's assessment of the enablement and argue that the claims are directed to what is done with information from the crystal once formed.

Applicants arguments filed 10/25/06 have been fully considered, but they are found unpersuasive. At the hart of the claimed invention is a protein crystal of PYK2. The crystal of SEQ ID NO: 1 described and enabled in the specification is the invention. It is not possible to separate the crystal from the information obtained from the crystal because no one can obtain information about the crystal without the crystal. Thus, the enablement issue of method of using the information of the crystal should be limited to the information taught about the crystal in the specification. The specification has enabled only one crystal of the polypeptide of SEQ ID NO: 1. Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation. The previous Office action sets out a *prima facie* case of non-enablement, explaining by sound scientific reasoning why a person of ordinary skill in the art would doubt that the guidance of the specification would enable practice of the full scope of the claimed invention without undue experimentation. Applicants have presented no evidence or, indeed, any arguments to establish the adequacy of the disclosure to enable the scope of the instant claims. Applicants merely assert that they disagree with the examiner and protein crystallization is routine in the art. Applicants make no effort to explain why they consider the disclosure of a structure of the protein of SEQ D NO: 1 crystallizes in specific crystal form to be enabling with respect to any crystal structure for any protein named PYK2 having any amino acid sequence or fragment thereof. Conclusory statements unsupported by evidence or scientific reasoning are insufficient to overcome the *prima facie* case of non-enablement set out in the previous Office action. New claims 99-104 are included in this rejection because they have the same enablement issue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 2, 5, 6, 8-16, 55, 66, 79-87, and 99-104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

(a) Claim 1 is incomplete for omitting essential method steps, such omission amounting to a gap between the steps for the reasons set forth in the prior Office action 6/22/06.

In response, applicants assert that the method does not require the steps indicated in the previous Office action, and that the orientation of the molecule can be determined from the structure information.

Applicants arguments filed 10/25/06 have been fully considered, but they are found unpersuasive. It appears hat the claim has multiple interpretations, which makes it indefinite. Applicants may wish to clarify in the claim how the orientation would be determined, i.e., *in silico* or *in vitro*.

(b) The phrase "with low or very low affinity", in amended claims 2 and 16, is a relative term, which render the claim indefinite. The specification does not define the phrase and one of ordinary skill in the art would not be able to ascertain the degree binding to call it a week binding. While applicants assert that the specification define the term, the examiner could not find a well-defined meaning to the phrase in the specification. Indefinite definition of the phrase would make the phrase and the claim indefinite.

(c) Claims 8, 12, and 55 are incomplete for omitting essential method steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to identify a compound that binds to PYK2.

In response, applicants assert that the method of identifying compound is not essential to the claim.

Applicants arguments filed 10/25/06 have been fully considered, but they are found unpersuasive. Contrary to the applicants' opinion, the methods of identifying the compound are essential to the claim. In fact, there are no numerous methods of identifying compounds that interact specifically with residues 503, 505, 457, 488, 567, and 554 of a protein called PYK2. Claims 12 and 55 as amended are included in this rejection because they suffer from the same deficiency.

(d) Claim 66 as a whole is incomplete, and therefore, is considered indefinite because the resulting claim does not define the metes and bound of the desired patent protection. The phrases "forming

the biological agent from the substructure" are indefinite terms and one of ordinary skill in the art would not know the metes and bound of these terms. It is not clear to this examiner how one of ordinary skill in the art would form the biological agent from a sub-structure and an antibody.

(f) The phrase "energetically allowed sites" in claim 79 renders the claim indefinite because the resulting claim does not set forth the metes and bound of the claimed invention. There are no absolute standards in the art of ascertaining the energy allowed sites from those, which are forbidden. The phrase is a relative term and subject to interpretation of individuals and therefore, the claim is indefinite.

Applicants argue that the rejection is confusing. The examiner agrees and corrected the typographical error.

(g) Claims 5, 6, 9-15, 80-87, and 99-104 are included with these rejection because they are dependent on rejected claim and do not cure its deficiencies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5-16, 55, 66, 72-87, and 99-104 are rejected under 35 U.S.C. 103(a) as being unpatentable over the commercial availability of computers and various software packages the structure of a candidate compound to the structure a protein such as PYK2, see for example U. S. patent 6,197,495 ('495, Qiu *et al.*), in view of U. S. patents 5,837,524 ('524, Schlessinger *et al.*) and U. S. patent 6,100,254 ('254, Budde *et al.*) for the reasons set forth in the prior Office action mailed June 22, 2006.

In response to the above rejection, applicants disagree with the examiner's rejections and argue that the prior art does not teach modifying the compound as required by independent claims 8, 12, and 55. Also, applicants argue that, while the '254 patent teaches a broad range of compounds, the reference provide no direction to select compound with a triazol R group, and that claim 72 require the modification of formula I.

Applicants arguments filed 10/25/06 have been fully considered, but they are found unpersuasive. While it is true the '495 patent does not specifically teach modifying known inhibitor for specific activity using the three-dimensional structure, said use is well-known in the prior art and is part of identifying more specific inhibitors for a specific enzymatic activity. The '245 patent teach several chemical structures and their derivative as inhibitors of tyrosine kinases including formula I. Thus, it would have been obvious to one of ordinary skill in the art to use a known inhibitor of the tyrosine kinase activity and use the three-dimensional structure to modify the known inhibitor to improve its inhibition specificity. In fact, it is an established routine in any drug discovery program that the three-dimensional structure suggests an initial lead compound, which is further modified through an iterative process. The iterative process includes the synthesis of said structure, determine it inhibition of the target protein, and use the three-dimensional structure again to improve the first compound binding and selectivity for the target protein. See IDS reference Cohen *et al.*, the paragraph bridging pages 883-884. The motivation of identifying compounds that bind to and inhibit PYK2 is found in the '459 patent. Thus, it would be obvious to one of ordinary skill in the art to select chemical structure of compounds that are known in the prior art to inhibit protein tyrosine kinases. The '245 patent is not required to identify the compound of formula I as more desired than any other to establish a *prima facie* case of obviousness or that compounds of formula I are inhibitors of PYK2. There is no apparent disagreement between the examiner and the applicants regarding the teaching of the '245 patent.

With regard to claim 66, the motivation to obtain antibody was stated in the prior Office action, which is to identify a specific antibody for diagnostic purposes. Similarly, the ordinary skill in the art would have a motivation to identify a sterically unhindered site in a PYK2 binding compound to attach the binding compound through a linker to a solid support to use as an affinity solid support for purifying PYK2 to be used in the method of identifying compounds. Again attaching binding compound to a solid support for the purpose of affinity purification of proteins is well known in the prior art.

No claim is allowed.

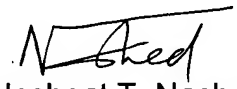
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1656